Development of Laser-generated Surface Acoustic Wave Immuno-sensors

Synopsis

Surface Acoustic Wave (SAW) devices have emerged as promising candidates for the advancement of rapid, low-cost, lab-on-chip point-of-care biosensors (*Zida et al. 2021*). These biosensing devices offer potential for early disease diagnosis and biomarker monitoring due to their sensitivity in detecting small variations in mechanical properties (i.e. changes in mass, density, rigidity, viscosity) resulting from cellular processes such as division, differentiation, communication and death, as well as subcellular events like DNA replication, protein folding, and organelle biogenesis. However, existing SAW biosensors typically rely on bulky piezoelectric substrates with interdigitated electrodes, which often lack biocompatibility and operate at fixed acoustic frequencies, limiting their sensitivity and agility. Additionally, integrating and interfacing such devices with other biomedical and microfluidic systems poses significant challenges due to their unwieldy electronic settings.

To address these limitations, opto-acoustic techniques present an alternative approach. These techniques utilize laser light to generate and probe high frequency ultrasonic waves (*Chen 2016*). In this project, we propose to leverage opto-acoustic schemes to design and develop a laser-based SAW biosensor operating over a wide frequency spectrum, ranging from tens of MHz up to a GHz. We will use laser-induced diffraction gratings to excite and probe these high-frequency SAWs remotely (*Vega-Flick et al. 2015)*, without the need of interdigitated piezoelectric transducers. This biosensor aims to enable fast and efficient detection of cellular and biomolecular processes, including specific antibody-antigen binding events, serving as a proof of concept. Since the sensing mechanism of SAW devices relies primarily on mass-loading to detect binding events, resolution can be limited by the low mass of molecular antibodies. To enhance signal detection and render our sensor more sensitive, we propose to use functionalized biocompatible and biodegradable micro-droplets (*Montel et al. 2015)* as signal amplifiers. Droplets functionalized with antibodies will bind specifically the antigen and enhance the mass-loading by several orders of magnitude. The adhesion of the droplet on the antigen-covered surface will additionally allow us to measure the antigen-antibody binding energy. Finally, we will leverage our droplet-assisted sensitive SAW immuno-sensor to detect typical autoantibodies associated with autoimmune disorders (*Schlichtiger et al. 2012*), such as those found in rheumatoid arthritis, type I diabetes, and systemic lupus erythematosus.

As part of this, the doctoral candidate will i) design and fabricate an all-optical SAW sensor using numerical tools and microfabrication techniques, ii) characterize the performance and sensitivity of the sensor and identify its optimal parameters and configuration using optoacoustic setups and analytical/numerical analysis, iii) perform the

biochemical protocols needed for the functionalization of the sensor surface and signal amplifiers, and iv) measure and analyze the immuno-sensing performance of the biosensor.
The proposed doctoral thesis, which aims at developing novel SAW biosensors for the next generation micro/nano diagnostics technologies, is highly interdisciplinary, and draws upon concepts from applied physics, mechanical and materials engineering, physical chemistry, as well as immunology and life sciences. Throughout this project, the doctoral candidate will be part of the Biophysics team at Institut Lumière Matière (ILM). The identification and preparation of autoantibodies for the evaluation of the sensor's performance as well as the detection of autoimmune disorders will be developed in collaboration with immunologists at the Centre International de Recherche en Infectiologie (CIRI). We also envision connecting with ArchiFun's industrial partners, such as NanoTemperTech, NovAlix, and Fida Biosystems, whose expertise in biosensing and diagnostics could facilitate the translation of these novel technologies into commercial devices. We anticipate that these collaborations, along with the thesis's interdisciplinary nature, will contribute significantly to the doctoral candidate's research profile, laying a solid foundation for their future professional career.

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Proposed partners for secondments:
NanoTemperTech, NovAlix and Fida Biosystems

Main ArchiFun theme involved:

Neurodegenerative and autoimmune diseases;